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Original Article

Risk factors for axillary lymph node metastasis in breast cancer

Eray Kurnaz[1], Bilgin Celebi[2], Banu Karapolat[3], Huseyin Eken[1], Uzer Kucuktulu[3]

[1]Erzincan Binali Yidirim University, Faculty of Medicine, Department of General Surgery, Erzincan, Turkey
[2]Ankara Dikmen 29 Mayıs State Hospital, Clinic of General Surgery, Ankara, Turkey
[3]University Of Health Science, Trabzon Kanuni Training Hospital, Department of General Surgery,Trabzon, Turkey

Abstract

Aim: As well as in Turkey as in the rest of the World, breast cancer is an increasing health problem. Although the axillary lymph node dissection is seen as an integral part in the breast cancer treatment, for it provides staging and local control, it also leads to complications and morbidity.

Material and Methods: We retrospectively reviewed the file of 286 patients which operated with breast cancer by January 2006 to January 2017. We researched and tried to find factors that influence the axillary lymph nodes.

Results: At 166 patients' axillary lymph nodes has been found (58%). Literature shows factors that have a positive effect on axillary lymph node; age of patients, tumor location, and tumor histopathology and tumor size. We evaluated the above stated parameters with statistical systems.

Conclusion: Tumor size which is larger than 2 cm and invasive ductal carcinoma histopathology are risk factors on the axillary lymph node metastases.

Keywords: Breast cancer; lymph node; risk factors.

INTRODUCTION

Breast cancer is the most common malign tumor of women; approximately 30% of all cancers seen in women and 18% of cancers related deaths in women (1). Breast cancer in developing countries is growing at a great rate. As a result, a large number of studies have been carried out on the etiology, early diagnosis, treatment, and genetic sub-structure, post-treatment complications of breast cancer, and to reduce and treat these complications (2). Being a woman, being over 30 years old, having a long menstrual cycle, becoming pregnant after 30 years, having a cancer of the other breast, feeding on a fat and calorie diet, colon and endometrium cancer, atypical hyperplasia in the mammary, lobular and ductal carcinoma in situ are the risk factors. There is also high risk in those with family history and carrying BRCA-1 or BRCA-2 gene mutations (3). We aimed to determine the parameters that will affect axillary lymph nodes by retrospectively evaluating the patients who were operated on in our clinic. When the number of metastatic lymph nodes was thought to affect postoperative follow-up and treatment significantly, it was investigated which parameters were best evaluated in patient follow-up to affect long-term survival.

MATERIAL and METHODS

Two hundred eighty-six female patients with stage 1, 2 and 3 breast cancer who underwent surgery on 1st January 2006 to 31st January 2017 were included in the study. The study was prepared in the form of retrospective file scanning. Written informed consent was taken from all of the patients. Ethics committee approval was obtained for the study.

The main inclusion criteria for the study were the axillary dissection, regardless of the surgical procedure. Retrospective screening of our databases revealed information on patients who had axillary dissection. Male patients were excluded from the study. Sentinel lymph node negative patients, those in carcinoma in situ histopathology, patients receiving neo-adjuvant treatment, patients who have only lumpectomy or simple mastectomy were not included in the study. The age at

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Corresponding Author: Eray Kurnaz, Erzincan Binali Yidirim University, Faculty of Medicine, Department of General Surgery, Erzincan, Turkey, **E-mail:** eraykurnaz52@hotmail.com

diagnosis, the size of the tumor, histopathologic features of the tumor, the total number of axillary lymph nodes and the number of metastatic lymph nodes were recorded. Patients were divided into two groups; over 40 year-old and under 40 years old (4). Anatomically, the breast was divided into five parts, the upper outer, the upper inner, the lower outer, the lower inner and the central quadrants (5). Tumor location was recorded according to these regions. Pathology reports were based on tumor diameters. Patients were divided into two groups with a pathologic tumor diameter of 2 cm above and below. Patients whose pathology results were only reported as invasive carcinoma were evaluated. Patients were divided into two groups as invasive ductal carcinoma and invasive non-ductal carcinoma.

Work data saved to Excel file. Data were analyzed and transferred to SPSS 23.0 (Statistical Package for Social Sciences). The normal distribution of the data was evaluated by the Shapiro Wilk test. Numerical data corresponding to normal distribution are presented as mean + -SD, and numerical data that do not correspond to normal distribution are presented as median (min-max). Categorical data were expressed in n, %. Student t test was used for the normal distribution in the numerical data and Mann Whitney U test was used in the absence of the normal distribution. Chi-square test was used to compare categorical variables. p <0.05 was considered significant.

RESULTS

Axillary metastatic lymph nodes were not detected in 120 of 286 patients included in the study. In 166 patients, there were 1 or more metastatic lymph nodes. It was seen that the maximum lymph nodes removed from the ipsilateral axilla was 47 and the minimum lymph nodes was 5, median 18 (5-47). At least 1, at most 36 lymph nodes were removed in axillary lymph node metastasis positive patients. The mean age of the patients was 54.4, median age 51 (21-88). Patients were divided into two groups; over 40 years old and under 40 years old. Axillary lymph node metastasis was detected in 67.5% (n = 29) of 43 patients under 40 years of age. Axillary lymph node metastasis was detected in 56.4% (n= 137) of 243 patients over 40 years of age (Table 1).There was no significant difference between the axillary lymph node metastasis rates according to age groups (p = 0.175).

Table 1. Distribution of Axillary Lymph Node Metastases According to Age Groups of Patients

AGE	AMLN -	AMLN +	Total
<= 40	14. 32.5%	29. 67.5%	43
>40	106. 43.6%	137. 56.4%	243
TOTAL	120	166	286

AMLN: Axillary Metastatic Lymph Nodes

There was no difference in the rates of axillary lymph node metastasis in patients under 40 years of age and in patients over 40 years of age.

Tumor diameters were evaluated based on the patient's pathology reports. When the patients are evaluated according to their tumor diameters; the diameter of the smallest tumor was 0.4 cm, the diameter of the largest tumor was 13 cm, median 2.5 (0.4-13). Mean tumor diameter was 3.1 cm. Patients were divided into two groups according to tumor diameter smaller than 2 cm (T1 according to the AJCC-TNM staging system) and larger than 2 cm. Axillary lymph node metastasis was detected in 46.3% (n = 50) of 108 patients with a tumor diameter less than 2 cm. Axillary lymph node metastasis was detected in 65.2% (n = 116) of 178 patients with tumors larger than 2 cm in diameter (Table 2).

Table 2. Distribution of Axillary Lymph Node Metastases According to Tumor Diameters of Patients

Tumor Diameter (cm)	ALMN -	ALMN +	Total
<= 2	58. 53.7%	50. 46.3%	108
>2	62. 34.8%	116. 65.2%	178
Total	120	166	286

AMLN: Axillary Metastatic Lymph Nodes

There was a statistically significant difference between axillary lymph node metastasis rates according to tumor diameters (p = 0.001). When the tumor diameter is over 2 cm, metastatic axillary lymph node risk increases.

The breast was anatomically divided into five quadrants and the tumor locations were grouped. When the patients were evaluated according to tumor localization; the most frequent involvement was the upper-outer quadrant (n: 171 59.8%). The region with the least involvement was the lower-inner quadrant (n: 11, 3.8%). When axillary lymph node metastases are evaluated together; the most frequent axillary involvement was found in centrally located tumors (75%), and at least axillary involvement was found in the upper-inner quadrant tumors (51.7%) (Table 3)

Table 3. Distribution of axillary lymph node metastases according to tumor localization of patients

Tumor Location	ALMN -	ALMN +	Total
Upper-Outer Quadrant	75. 43.9%	96. 56.1%	171
Upper-Inner Quadrant	14. 48.3%	15. 51.7%	29
Lower-Outer Quadrant	21. 44.7%	26. 55.3%	47
Lower-Inner Quadrant	3. 27.3%	8. 72.7%	11
Central	7. 25%	21. 75%	28
Total	120	166	286

AMLN: Axillary Metastatic Lymph Nodes

There was no statistically significant difference between axillary lymph node metastasis rates according to tumor localization (p = 0.272).

Histopathological examinations revealed 7 different pathologic cell groups in the patients. The most common group was invasive ductal carcinoma (n=241, 84.2%). The least common cell type was invasive tubular carcinoma (n=2 0.7%). Other cell types are; invasive lobular carcinoma (n=11 3.8%), invasive ductal-lobular (mix cell type) carcinoma (n=11 3.8%), invasive mucinous carcinoma (n=10 3.5%), invasive papillary carcinoma (n=6 2.1%), invasive medullary carcinoma (n=5 1.7%). In terms of statistical analysis, patients were divided into two groups as invasive ductal carcinoma and other invasive carcinomas (Table 4).

Table 4. Distribution of Axillary Lymph Node Metastases According to Histopathological Characteristics

Tumor Histopathology	ALNM -	ALNM +	Total
Invasive Ductal Carcinoma	95. 39.5%	146. 60.5%	241
Other Invasive Carcinomas	25. 55.6%	20. 44.4%	45
Total	120	166	286

AMLN: Axillary Metastatic Lymph Nodes

A statistically significant difference was found between axillary lymph node metastasis rates according to tumor histopathology (p=0.044). Invasive ductal carcinoma histopathologic features of the tumor increase the risk of axillary lymph node metastasis.

DISCUSSION

Breast cancer is a heterogeneous disease in which epigenetic and genetic changes are affected by progressive accumulation of hereditary and environmental risk factors (6). The general aim of breast cancer surveys is to identify prognostic and predictive changes (7). Age is the most important independent risk factor for this disease in which dependent and independent risk factors are active at various levels. The incidence of breast cancer increases with age. The incidence curve rises steeply as menopause doubles in every decade. The disease is plateaued at age 50 and then rises upright again. This curve is significantly affected by ovarian activity. Breast cancer is more common in the postmenopausal period (8). More than 80% of patients with breast cancer are over 40 years of age. In a study of 1381 cases, the number of breast cancer cases in the age group of 40-70 years constituted 67.5% of all cases (9). The incidence of breast cancer is lower in the premenopausal period (10). Breast cancer is most commonly seen in the upper outer quadrant of the mammary gland. The rate of occurrence in this area is 50-60%. Tumors are found 10% in the upper inner quadrant, 10% in the lower outer quadrant, 10% in the lower inner quadrant and 20% in the areolar region. In a previous study, it was reported that primary tumor localization did not affect prognosis for patients undergoing both radical surgery and breast converting surgery (11). It was investigated that the cause of breast cancer to be seen more frequently in the upper outer quadrant and examined the results of 746 breast biopsies taken from different quadrants. Biopsy results classified as normal, benign and malignant lesions. The reason for the malignant lesions to be seen more frequently in the upper outer quadrant is due to the presence of more breast tissue in the upper outer quadrant (12). Reported no association between tumor localization and prognosis suggests that rates of breast tumor localization offer only data to be considered during breast examination. An advantage for breast conserving surgery is that the breast tumor is localized more frequently on the upper outer quadrant (13). One of the prognostic factors used in the follow-up of breast cancer is histopathologic type of tumor. Breast cancer is histopathologically divided into invasive and in situ carcinoma. Invasive ductal carcinoma is the most common histopathologic subtype of invasive carcinomas (75-80%). The other subtypes are invasive lobular (5-15%), tubular (2%), mucinous (1-6%), medullary (1-2%) and less frequently mixed type (14). Primary tumor diameter is an important and reliable prognostic factor for the risk of recurrence in breast cancer and selection of adjuvant treatment, especially in node-negative patients (15). Tumor diameter affects axillary node involvement. As the diameter increases, axillary involvement and the number of nodes retained increases. The prognosis of small diameter tumors with axillary involvement is better than that of large diameter tumors. In all nodal involvement categories the survival is shortened as the tumor diameter increases (16). The most important factor in determining the prognosis of breast cancer and the treatment protocol to be applied is the status of axillary lymph nodes. For this reason, axillary dissection is important in accurately staging breast cancer and determining the adjuvant treatment to be performed. Metastatic involvement detected in axillary lymph nodes on histological examination is the strongest prognostic factor in patients with primary breast cancer (17). It was found that lymph node involvement of 4 and above significantly reduced survival (18). In this study, axillary nodal involvement; 51.6% in 60 cases with T1 tumors, 59.4% in 101 cases with T2 tumors, 51.2% in 41 cases with T3 tumors and 100% in 10 cases with T4 tumors. There is a positive correlation between tumor size and axillary node involvement.

CONCLUSION

Axillary lymph node dissection is still accepted as the gold standard in many centers for evaluating axilla. However, the increase in our knowledge of tumor biology, the increased recognition of breast cancer at an earlier stage and the initiation of more conservative treatment, the increased indications for systemic adjuvant treatment, the increased success with these treatments, and the better understanding of axillary lymph node dissection complications, the necessity of routine axillary lymph

node dissection should be questioned. In recent years, initiatives that provide information and benefits from axillary lymph node dissection but have lower morbidity have come into use (such as sentinel lymph node biopsy). It is important to identify patients with a low risk of axillary lymph node involvement and to identify patients whose axillary lymph node status will not change the treatment scheme. As a result of our study, we obtained two predictive factors that are effective for axillary lymph node metastasis. If the tumor is more than 2 cm in diameter and invasive ductal carcinoma is present, axillary lymph node metastasis risk increases. When these results are supported by more extensive studies, they can help us to clinical support for our patients.

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Eray Kurnaz ORCID:0000-0002-9043-558X
Bilgin Celebi ORCID:0000-0002-2127-0005
Banu Karapolat ORCID:0000-0001-5132-8266
Huseyin Eken ORCID:0000-0001-6095-6002
Uzer Kucuktulu ORCID:0000-0003-4481-9176

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